

AMENDMENTS TO THE CLAIMS

Please replace the claims with the claim listing provided below.

1. (Currently Amended) A method of countering the development of resistance in a parent target to a parent neutralizing agent, wherein said parent target is an antigen and said parent neutralizing agent is an antibody that neutralizes said antigen or countering the development of neutralizing activity in a parent neutralizing agent to a parent target comprising coevolving said parent target and said parent neutralizing agent, wherein said coevolving comprises

1) diversifying each of said parent target and said parent neutralizing agent in vitro to produce a diversified target population,

2) selecting one or more next generation targets from said diversified target population, wherein the selected one or more next generation targets has increased resistance to said parent neutralizing agent,

3) diversifying said parent neutralizing agent in vitro to produce a diversified neutralizing agent population,

4) selecting one or more next generation neutralizing agents from said diversified neutralizing agent population wherein said next generation neutralizing agents have increased neutralizing activity against said one or more next generation targets, and

5) optionally repeating said diversifying and selecting of steps 1) to 4) using said next generation neutralizing agents and next generation targets,

wherein selection of said one or more next generation neutralizing agents in step 4) counters the development of resistance in said parent target.

2. (Original) The method of claim 1 wherein said diversifying comprises generating a population of targets and neutralizing agents by mutagenesis, recombinant methods, or combinatorial synthetic methods.

3.- 50. (Canceled)

51. (New) The method of claim 1 wherein said antigen is a preventative antigen.
52. (New) The method of claim 1 wherein said antibody is a monoclonal antibody.
53. (New) The method of claim 1 wherein said antigen is derived from a virus.
54. (New) The method of claim 53 wherein said antigen is derived from RSV.
55. (New) A method of coevolving a parent target and a parent neutralizing agent to form a next generation neutralizing agent with new or improved neutralizing activity against a next generation target, wherein said parent target is an antigen that is neutralized by said parent neutralizing agent which is a protein, comprising:
- a) diversifying in vitro said parent target and selecting at least one next generation target from a diversified population of targets resulting from said diversifying, wherein the selected at least one target has new or improved resistance to a parent neutralizing agent having neutralizing activity against said parent target; and
- b) diversifying in vitro said parent neutralizing agent and selecting at least one next generation neutralizing agent from a diversified population of neutralizing agents resulting from the diversifying, wherein the selected at least one neutralizing agent has new or improved neutralizing activity against the selected at least one target,
- wherein said diversifying and selecting of steps a) and b) form a next generation neutralizing agent with new or improved neutralizing activity against said next generation target.
56. (New) The method of claim 55 wherein said protein is a protein that binds to said antigen.
57. (New) The method of claim 55 wherein said protein is an antibody.
58. (New) The method of claim 55 wherein said protein comprises a PDZ domain.

59. (New) A method of countering the development of resistance in a parent antigen to a parent protein, wherein said parent protein comprises a PDZ domain that binds to said parent antigen and neutralizes said parent antigen, comprising coevolving said parent antigen and said parent protein, wherein said coevolving comprises:

- 1) diversifying said parent antigen in vitro to produce a diversified antigen population,
- 2) selecting one or more next generation antigens from said diversified antigen population, wherein the selected one or more next generation antigens has increased resistance to said parent protein,
- 3) diversifying said parent protein in vitro to produce a diversified protein population,
- 4) selecting one or more next generation proteins from said diversified protein population, wherein said next generation proteins have increased neutralizing activity against said one or more next generation antigens, and
- 5) optionally repeating said diversifying and selecting of steps 1) to 4) using said next generation proteins and next generation antigens,
wherein selection of said one or more next generation proteins in step 4) counters the development of resistance in said parent antigen.

60. (New) The method of claim 59 wherein said parent antigen is a protein containing a C-terminus to which the PDZ domain of said parent protein binds.